## Acknowledging Receipts? New Evidence for Dermal Absorption of Bisphenols

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Bisphenol A (BPA) is perhaps the archetypal endocrine-disrupting chemical (EDC). Due to the chemical's use in canned food and certain beverage containers, many researchers have focused on oral exposure routes for BPA and its ostensibly safer substitutes, such as bisphenol S (BPS). But BPS and BPA are also used as developers in receipts and other thermal papers, raising the potential for dermal exposure. A recent study in *Environmental Health Perspectives* adds to the evidence that people who handle thermal receipts absorb these compounds through their skin.

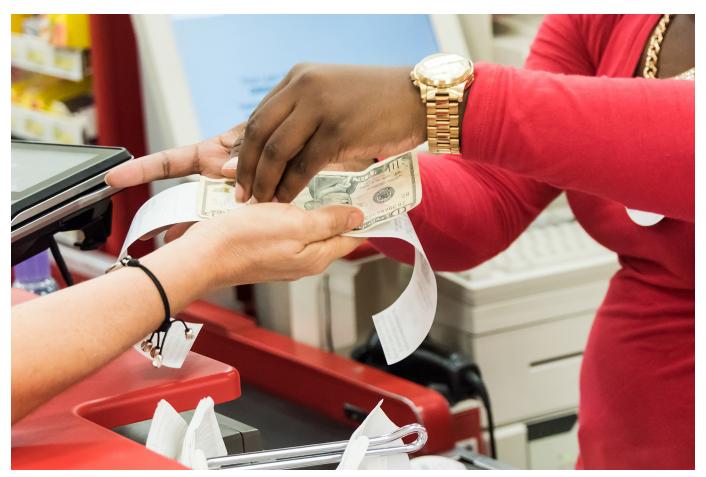
Two investigators tested BPA and BPS in an *in vitro* human skin cell model and found that the former crossed skin more efficiently than the latter. This was consistent with their companion experiment in which five male volunteers handled simulated (for BPA) and authentic (for BPS) store receipts for 5 minutes each.

Despite lower percutaneous absorption, the average percentage of free BPS in the men's urine was higher (6.9%) than that of free BPA (2.7%) up to 48 hours after exposure. Thus, less BPS than BPA was metabolized in the body. This has potential human health implications because—like BPA—BPS has endocrine-active properties,<sup>3</sup> and only free, unmetabolized bisphenols bind to estrogen receptors.<sup>4,5</sup>

"Our study is a mix of good and bad news," says coauthor Jonathan Martin, a professor of environmental toxicology at Sweden's Stockholm University. "The good news is that BPS crosses your skin [more slowly] and perhaps to a lesser extent than BPA. But that does not mean fewer [potential] health concerns, because less of that BPS is detoxified." Evaluating the balance of these results will require a much larger risk assessment study, Martin adds.

Earlier, Martin and coauthor Jiaying Liu, a postdoctoral fellow in urban and environmental sciences at Peking University, had reported<sup>6</sup> that dermal absorption of BPA resulted in longer systemic circulation than dietary exposures in a study of six male participants. After manual handling of receipts, urinary excretion of BPA increased linearly for 2 days, and some participants still had detectable BPA levels after 1 week. In contrast, the same group cleared all dietary BPA within 24 hours.

To follow up on these findings, Liu and Martin studied BPS, a common BPA substitute in thermal paper<sup>7</sup> that can also transfer readily onto paper currency.<sup>8</sup> Other investigators—in small studies in the United States,<sup>9</sup> Canada,<sup>10</sup> and Italy<sup>11</sup>—have measured BPS in approximately half of store receipts sampled from actual



Receipts printed on thermal paper are believed to be a common source of bisphenol exposures in people, with cashiers receiving especially high estimated exposures. When people store their receipts alongside their cash, the chemicals can transfer onto the paper, making currency another ready source of potential exposure. \*\*B.18\*\* Image: © iStockphoto/Juanmonino.

stores. Occupational studies, also with small sample sizes, have detected higher urinary BPS levels in cashiers after their shifts compared with pre-shift levels and with noncashiers. <sup>12,13</sup>

"To my knowledge, this is the first study to demonstrate that BPS crosses the human skin," says Ana Soto, an endocrinologist at Tufts University. "It shows that people who handle receipts excrete BPS in their urine, which supports the importance of dermal exposures to BPS and other EDCs." She adds that multiple exposure routes are additive, raising concerns not only for cashiers, but also people who handle receipts or paper currencies just prior to consuming finger foods. Soto was not involved in the new study.

An independent recent study<sup>14</sup> compared the metabolism of orally ingested BPS and BPA in piglets, whose toxicokinetic pathways are similar to humans'.<sup>15</sup> Consistent with previous work, <sup>16,17</sup> the investigators estimated that systemic exposure to BPS was about 250 times higher than to BPA after oral dosing due to reduced metabolism. Véronique Gayrard, a professor of physiology at the National Veterinary School of Toulouse and first author of the piglet paper, suggests that replacing BPA with BPS in food and beverage containers may increase human exposure to hormonally active compounds. "These two analyses<sup>2,13</sup> are difficult to compare because they concern two different exposure routes in two different organisms," says Gayrard, who was not involved in the new study. However, she adds, both studies emphasize the importance of toxicokinetic studies for BPA substitutes.

In the case of BPS, Liu concludes, this should go beyond dietary exposures. "More studies of dermal exposure routes are warranted because their contribution to total human exposure may have been underestimated," she says.

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## References

- Schug TT, Johnson AF, Birnbaum LS, Colborn T, Guillette LJ, Crews DP, et al. 2016. Minireview: endocrine disruptors: past lessons and future directions. Mol Endocrinol 30(8):833–847, PMID: 27477640, https://doi.org/10.1210/me.2016-1096.
- Liu J, Martin JW. 2019. Comparison of bisphenol A and bisphenol S percutaneous absorption and biotransformation. Environ Health Perspect 127(6):67008, PMID: 31199677, https://doi.org/10.1289/EHP5044.
- Rochester JR, Bolden AL. 2015. Bisphenol S and F: a systematic review and comparison of the hormonal activity of bisphenol A substitutes. Environ Health Perspect 123(7):643–650, PMID: 25775505, https://doi.org/10.1289/ehp.1408989.
- Matthews JB, Twomey K, Zacharewski TR. 2001. In vitro and in vivo interactions
  of bisphenol A and its metabolite, bisphenol A glucuronide, with estrogen receptors α and β. Chem Res Toxicol 14(2):149–157, PMID: 11258963, https://doi.org/10.
  1021/tx0001833.

- Snyder RW, Maness SC, Gaido KW, Welsch F, Sumner SC, Fennell TR. 2000. Metabolism and disposition of bisphenol A in female rats. Toxicol Appl Pharmacol 168(3):225–234, PMID: 11042095, https://doi.org/10.1006/ taap.2000.9051.
- Liu J, Martin JW. 2017. Prolonged exposure to bisphenol A from single dermal contact events. Environ Sci Technol 51(17):9940–9949, PMID: 28759207, https://doi.org/10.1021/acs.est.7b03093.
- Björnsdotter MK, de Boer J, Ballesteros-Gómez A. 2017. Bisphenol A and replacements in thermal paper: a review. Chemosphere 182:691–706, PMID: 28528315, https://doi.org/10.1016/j.chemosphere.2017.05.070.
- Liao C, Liu F, Kannan K. 2012. Bisphenol S, a new bisphenol analogue, in paper products and currency bills and its association with bisphenol A residues. Environ Sci Technol 46(12):6515–6522, PMID: 22591511, https://doi.org/10.1021/es300876n.
- Hormann AM, vom Saal FS, Nagel SC, Stahlhut RW, Moyer CL, Ellersieck MR, et al. 2014. Holding thermal receipt paper and eating food after using hand sanitizer results in high serum bioactive and urine total levels of bisphenol A (BPA). PLoS One 9(10):e110509, PMID: 25337790, https://doi.org/10.1371/journal.pone. 0110509
- Liu J, Wattar N, Field CJ, Dinu I, Dewey D, Martin JW, et al. 2018. Exposure and dietary sources of bisphenol A (BPA) and BPA-alternatives among mothers in the APrON cohort study. Environ Int 119:319–326, PMID: 29990952, https://doi.org/10. 1016/j.envint.2018.07.001.
- Russo G, Barbato F, Grumetto L. 2017. Monitoring of bisphenol A and bisphenol S in thermal paper receipts from the Italian market and estimated transdermal human intake: a pilot study. Sci Total Environ 599–600:68–75, PMID: 28463702, https://doi.org/10.1016/j.scitotenv.2017.04.192.
- Thayer KA, Taylor KW, Garantziotis S, Schurman SH, Kissling GE, Hunt D, et al. 2016. Bisphenol A, bisphenol S, and 4-hydroxyphenyl 4-isoprooxyphenylsulfone (BPSIP) in urine and blood of cashiers. Environ Health Perspect 124(4):437–444, PMID: 26309242, https://doi.org/10.1289/ehp.1409427.
- Ndaw S, Remy A, Denis F, Marsan P, Jargot D, Robert A. 2018. Occupational exposure of cashiers to bisphenol S via thermal paper. Toxicol Lett 298:106– 111, PMID: 29800715, https://doi.org/10.1016/j.toxlet.2018.05.026.
- Gayrard V, Lacroix MZ, Grandin FC, Collet SH, Mila H, Viguié C, et al. 2019. Oral systemic bioavailability of bisphenol A and bisphenol S in pigs. Environ Health Perspect 127(7):77005, PMID: 31313948, https://doi.org/10.1289/EHP4599.
- Kararli TT. 1995. Comparison of the gastrointestinal anatomy, physiology, and biochemistry of humans and commonly used laboratory animals. Biopharm Drug Dispos 16(5):351–380, PMID: 8527686, https://doi.org/10. 1002/bdd.2510160502.
- Oh J, Choi JW, Ahn YA, Kim S. 2018. Pharmacokinetics of bisphenol S in humans after single oral administration. Environ Int 112:127–133, PMID: 29272776, https://doi.org/10.1016/j.envint.2017.11.020.
- Karrer C, Roiss T, von Goetz N, Gramec Skledar D, Peterlin Mašič L, Hungerbühler K. 2018. Physiologically based pharmacokinetic (PBPK) modeling of the bisphenols BPA, BPS, BPF, and BPAF with new experimental metabolic parameters: comparing the pharmacokinetic behavior of BPA with its substitutes. Environ Health Perspect 126(7):077002, PMID: 29995627, https://doi.org/10. 1289/EHP2739.
- Liao C, Kannan K. 2011. High levels of bisphenol A in paper currencies from several countries, and implications for dermal exposure. Environ Sci Technol 45(16):6761–6768, PMID: 21744851, https://doi.org/10.1021/es200977t.